IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Serial No.	:	**10/668,573**
Filed	:	September 23, 2003
Applicant	:	Jonathan R. Coppeta, et al.
Title	:	Micro-Reservoir Osmotic Release Systems and Microtube Array Device
TC/AU	:	3767
Examiner	:	Elizabeth MacNeill
Docket No.	:	17509-0068
Customer No.	:	29052

APPEAL BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Pursuant to 37 C.F.R. § 1.191 and M.P.E.P. § 1205, Applicants appeal the Examiner's final rejection of all pending claims in the referenced application. The fee of $255.00 required under 37 C.F.R. § 41.20(b)(2) is submitted herewith. A Petition for an Extension of Time for one month, to December 28, 2007, also is submitted herewith, along with authorization to charge the fee for Petition to Deposit Account 19-5029.

I. Real Party in Interest

The real party in interest in this appeal is MicroCHIPS, Inc., a corporation of the State of Delaware, having a principal place of business at 6-B Preston Court, Bedford, Massachusetts 01730.

II. Related Appeals and Interferences

There are no appeals or interferences related to the appeal of the present application.

III. Status of Claims

Claims 14-29, 35, 36, and 39-47 are pending and stand finally rejected as set forth in the Office Action mailed July 2, 2007 ("the Final Office Action"). Claims 1-13, 30-34, 37, and 38 are canceled. The rejections of claims 14-29, 35, 36, and 39-47 are being appealed.

IV. Status of Amendments

No amendments have been filed subsequent to the Final Office Action.

V. Summary of Claimed Subject Matter

Independent claim 14 is drawn to a device for the controlled release of chemical molecules. The claimed device includes (i) an array of discrete microtubes constructed of a metal or an alloy, each microtube comprising a reservoir defined therein (Page 7, Lines 22-24; Page 15, Lines 28-30; Page 23, Lines 27-28; FIG. 10), (ii) a release formulation which comprises the chemical molecules, the chemical molecules being wholly contained in each reservoir (Page 16, Lines 10-25; FIGS. 7, 10, 11, and 12), (iii) a rupturable covering which closes an opening at a first end of each reservoir (Page 3, Line 24; Page 16, Lines 11-14; FIG. 7), and (iv) a means for rupturing the rupturable covering and positively displacing the release formulation through the opening at the first end, to release the chemical molecules (Page 3, Lines 24-27; Page 7, Lines 8-9).

Independent claim 19 also is drawn to a device for the controlled release of chemical molecules. The claimed device includes (i) an array of discrete microtubes, each microtube comprising a reservoir defined therein (Page 7, Lines 22-24; Page 23, Lines 27-28; FIG. 10), (ii) a release formulation which comprises the chemical molecules, the chemical molecules being disposed in each reservoir (Page 16, Lines 10-25; FIGS. 7, 10, 11, and 12), (iii) a rupturable

covering enclosing a first end of each reservoir (Page 3, Line 24; Page 16, Lines 11-14; FIG. 7), and (iv) a means for rupturing the rupturable covering and positively displacing the release formulation through the opening at the first end, to release the chemical molecules (Page 3, Lines 24-27; Page 7, Lines 8-9).

The means for rupturing and positively displacing recited in Applicants' claims is described in the specification at page 16, line 10-14; page 17, lines 12-17; page 18, line 16 to page 20, line 7; page 22, line 5 to page 23, line 12; and in FIGS. 7, 10, 11, and 12. The means may include an expansion material, shown as structures 226 or 306. The means may further include coating 308 which comprises a high electrical resistance material, or a heating pad 312, or an exothermic reaction coating 322. For instance, the means may comprise a layer of an expanding material together with a resistive heating element or resistive coating. (Page 4, Lines 4-10; Page 21, Lines 4-9). The expanding material may comprise an osmotic agent, whose expansion is driven by intake of a fluid. (Page 22, Lines 7-8; Page 17, Lines 15-17). Alternatively or in addition, the mean for rupturing and positively displacing may include a microtube with sidewall 402 made of a shape memory alloy ("SMA").

Claim 19 describes and claims that the release formulation is disposed between the layer of expanding material and the rupturable covering, that the expanding material can be activated to expand upon application of heat, and that the resistive heating element or resistive coating is for heating the end of the microtube distal the rupturable covering upon application of an electric current. (Page 3 Line 29 to Page 4 Line 10; Page 22, Lines 4-9).

VI. Grounds of Rejection to Be Reviewed On Appeal

The following grounds of rejection are presented for review:

Ground No. 1

Whether a *prima facie* case of anticipation has been established to support a rejection of claims 14-18, 20-29, 35, 36, and 39 over U.S. Patent No. 6,692,456 to Eppstein (hereinafter "Eppstein").

Ground No. 2

Whether a *prima facie* case of obviousness has been established to support a rejection of claims 19 and 42-47 over U.S. Patent No. 7,025,323 to Krulevitch et al. (hereinafter "Krulevitch") in view of U.S. Patent No. 5,797,898 to Santini, Jr. et al. (hereinafter "Santini").

Ground No. 3

Whether a *prima facie* case of obviousness has been established to support a rejection of claims 40 and 41 over Eppstein in view of U.S. Patent No. 4,111,202 to Theeuwes (hereinafter "Theeuwes").

VII. Argument

A. Background

Applicants' claimed invention pertains to devices and methods for the controlled release of chemical molecules, such as drug molecules for a therapeutic application. The claimed device require an array of microtubes each of which defines a reservoir therein, a release formulation stored in the reservoirs, a rupturable covering closing off an end opening in each reservoir, and a means for rupturing the rupturable covering and positively displacing the release formulation. As specified in the claims, the function of these means is to *positively displace* the release formulation out of the reservoir/device. Advantageously, the positive displacement can provide an increased rate of release of the chemical molecules as compared to the release

obtainable with passive diffusion alone (Page 6, Lines 21-25). In fact, such enhanced release kinetics may be necessary, for example, in releasing drugs whose efficacy is dependent on a fast pharmacokinetic pulsatile profile (Page 6, Lines 25-28).

B. Ground No. 1

The rejection of claims 14-18, 20-29, 35, 36, and 39 over Eppstein is erroneous. A proper *prima facie* case of anticipation has not been established to support the rejection.

Eppstein teaches devices for forming openings in biological membranes and delivering fluid therethrough using "pressure modulation links" "(a)" (Col. 31, Lines 19-23; Fig. 24). Specifically, the central pressure modulation links are pressed down relative to the outer links to compress the skin, and then the central links are pulled back while the outer links are pressed down to induce fluid to flow from the reservoir and into the skin (Col. 31, Lines 19-28; Fig. 22). The fluid in Eppstein's device is not positively displaced from the reservoir, as positive displacement requires that the space occupied by the fluid in the reservoir be eliminated (e.g., by reducing the dimensions and thus volume of the reservoir) or that the fluid be pushed out by another material (e.g., an expandable material) such that the fluid physically cannot remain in or return to the reservoir. In Eppstein, the reservoir volume is fixed and is not displaced by another material. Accordingly, Eppstein does not teach or suggest either structure or function for positively displacing a release formulation. Eppstein therefore fails to disclose, expressly or inherently, the positive displacement feature of Applicants' claims.

The Examiner has not met his legal burden to show that a single reference contains each and every element of the claims. An element in a claim expressed as a means for performing a specified function "shall be construed to cover the corresponding structure, material, or acts described in the specification or equivalents thereof." 35 U.S.C. § 112, ¶ 6. "Accordingly, the

PTO may not disregard the structure disclosed in the specification corresponding to such language when rendering a patentability determination." In re Donaldson Co., 16 F.3d 1189, 1195 (Fed. Cir. 1994). In making a *prima facie* case of equivalence, "the Examiner should provide an explanation and rationale in the Office Action as to why the prior art element is an equivalent." M.P.E.P. § 2183. Importantly, the application of a prior art reference to a means plus function claim *requires* that the prior art element perform the *identical function* specified in the claim. M.P.E.P. § 2182.

In the instant case, the Examiner has not set forth the required clear and particular showing of how the required "*means for rupturing* the rupturable covering *and positively displacing* the release formulation" is set forth in Eppstein. First, "unless an element performs the identical function specified in the claim, it *cannot* be an equivalent." M.P.E.P. § 2184 [II]. While the pyrotechnic element of Eppstein may provide a rupture function, it has no positive displacement function on the release formulation. Because neither the pressure modulation links nor any other structure in Eppstein performs the function of positively displacing a release formulation, they *cannot* be equivalent to Applicants' means for functionally displacing the release formulation.

The Examiner alleges that Fig. 24 of Eppstein teaches a means "(e)" for rupturing a covering and positively displacing a release formulation. (Office Action, July 2, 2006, Page 2, ¶ 2). This is incorrect. Means "(e)" comprises a thermal poration element (FIG. 23a; Col. 31, Lines 13-16). Eppstein teaches that thermal poration elements may porate the surface of the skin and simultaneously breach the lower surface of the reservoir (Col. 25, Lines 36-39). Thermal poration element "(e)" clearly does not perform any kind of positive displacement. Merely

making the skin surface more porous does not positively displace a release formulation from any reservoir in Eppstein. Accordingly, a proper *prima facie* case of equivalence has not been made.

Moreover, nothing in Eppstein can reasonably be construed as supporting a *prima facie* conclusion of equivalence. Factors sufficient to support a *prima facie* conclusion of equivalence include: (a) whether the prior art element performs the identical function specified in the claim in substantially the same way; (b) whether a person of ordinary skill in the art would have recognized the interchangeability of the element shown in the prior art for the corresponding element disclosed in the specification; (c) whether there are insubstantial differences between the prior art element and the corresponding element disclosed in the specification; and (d) whether the prior art element is a structural equivalent of the corresponding element disclosed in the specification. M.P.E.P. § 2184 [II]. With respect to factor (a), Eppstein's pressure modulation system does not perform the "positively displacing" function specified in Applicants' claims, and plainly does not function in the same way. As to factor (b), a person of ordinary skill would have recognized that Eppstein's pressure modulation system is not interchangeable with Applicants' claimed means, since the pressure modulation system only can be used in close proximity to a biological membrane. As to factors (c) and (d), there are substantial differences, both structural and functional, between a pressure modulation system and Applicants' claimed means which, in some embodiments, includes a fluid or heat swellable material. For example, the structure and function of Eppstein's device provides and relies upon microporation of a biological membrane. In contrast, Applicants' claimed device does not require such functionality or structure.

The Examiner's reply that "the specification only provides means for rupturing NOT means for rupturing AND DISPLACING" (Advisory Action, page 2) is plainly incorrect.

Applicants describe, for example, that the expansion of the expansion material or shape changing of the SMA microtube causes the release formulation to be positively displaced from the microtube and necessarily causes the rupturable covering to be ruptured. See, e.g., page 19, lines 16-18 ("In another embodiment, release of reservoir contents from the microtube is controlled by changing the shape of the microtube rather than by expanding a material inside the reservoir of the microtube."); page 17, lines 19-21 (describing that rupture of the rupturable covering is, in one embodiment, "due to expansion of the expansion material."). Rupture means and positive displacement means are both described in Applicants' specification and in fact are described in some embodiments as inextricably linked together.

Furthermore, it is unclear what the Examiner is attempting to establish with the comment that "[t]he means for rupturing (conductive element) is exactly the same as disclosed by the applicant" (Advisory Action, Page 2). Applicants can find no paragraph "0031" and Eppstein nevertheless fails to disclose the structures and functions of Applicants' claims, in that there is no means in Eppstein for positively displacing the release formulation. Accordingly, no proper *prima facie* case of anticipation has been established.

Claims 14-18, 20-29, 35, 36, and 39 therefore are novel over Eppstein.

C. Ground No. 2

The rejection of claims 19 and 42-47 over Krulevitch in view of Santini is erroneous. A proper *prima facie* case of obviousness has not been established to support the rejection.

Krulevitch discloses a system (FIGS. 7A and 7B) that may deliver drugs through microneedles 97 by pumping fluid from reservoirs 86-90 located in a *substrate* 80 that is not a microtube (Col. 8, Lines 12-30). The reservoirs are *remote from* the microneedles, and

Krulevitch does not teach locating reservoirs within the microneedles. Accordingly, Krulevitch does not remotely teach or suggest a microtube having a reservoir defined therein.

Furthermore, Krulevitch does not teach or suggest any type of *rupturable covering*, and clearly does not suggest a *microtube* that has a *rupturable covering* that *encloses a first end of each reservoir*. In fact, Krulevitch teaches completely different methods of sealing. Specifically, Krulevitch teaches that "channel sealing is *dependent* on selective poly (dimethylsiloxane) (PDMS) surface modifications," and that "[t]he polymer channel should be hydrophobic and pneumatic fluid should be hydrophilic when using hydrophilic reagents *or vice versa*... for [a] leak proof seal." (Col. 6, Lns. 56-60) (emphasis added). Because Krulevitch teaches sealing molecules that are either hydrophilic or hydrophobic by the use of a specific type of *polymer* located *in the substrate/channel structures*, it **teaches away** from sealing with a *metallic* cover at the *end of the microneedle*.

Santini discloses a microchip for releasing substances from reservoirs etched in a substrate (Col. 11, Lines 33-40; FIG. 4). Because Santini does not teach or suggest any microneedle or microtube structure, it plainly cannot provide the required teaching or well reasoned basis for one of ordinary skill in the art to place a rupturable covering over the end of a microtube.

A person of ordinary skill trying to enclose and controllably release chemical molecules has a nearly infinite variety of options to choose from. Thus, it would have required more than ordinary skill to leap from the prior art teachings of Krulevitch, alone or in combination with the prior art, to somehow derive Applicants' particularly claimed device. Furthermore, nothing in Krulevitch or Santini teaches or suggests either (i) a device in which a release formulation is disposed within *a reservoir that is defined inside a microtube*, or (ii) a *microtube* that has a

rupturable covering that *closes an opening at a first end of each reservoir* as is specifically required by Applicants' claims. Thus, even if one skilled in the art would have been motivated—and it is submitted that he or she would not have been—to combine Krulevitch and Santini, the references clearly fail to teach or suggest all the elements of Applicants' claimed device.

The Examiner has not met his legal burden. "[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." KSR Int'l Co. v. Teleflex Inc., 550 U.S. ___ (2007) (Slip Op. at 14). The Court further stated that "it will be necessary … to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an **apparent** reason to combine the known elements **in the fashion claimed**..." Id.

The Examiner has not set forth the required showing that all elements of Applicants' claim 19 are included in the prior art or would be combined in the fashion claimed. The Examiner has merely alleged that "Krulevitch teaches an array of discrete microtubes (97) defining a reservoir (86-90)..." (Office Action, July 2, 2006, Page 3, ¶ 2) (Office Action, February 12, 2006, Page 3, ¶ 3). This is incorrect and misleading. Microneedles 97 do not in any reasonable way "define" reservoirs 86-90, because the formulation reservoirs in Krulevitch are remote from the microneedles. The Examiner's argument that "claim 19 does not require the reservoir to be WHOLLY contained in the microtubes (compare to claim 14)" (Advisory Action, Page 2) is irrelevant to the establishment of whether the cited prior art teaches a microtube having a formulation storage reservoir defined therein. One of ordinary skill in the art would not

reasonably consider the Krulevitch microneedles to be reservoirs when the reference clearly refers to another remote structure as the reservoir for the drug that, in operation, passes briefly through the microneedle.

Furthermore, the Examiner has not set forth a showing as to why one of ordinary skill in the art would combine Krulevitch and Santini to derive Applicants' particularly claimed device. "A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning." KSR Int' l Co. v. Teleflex Inc., 550 U.S. ___ (2007) (Slip Op. at 17). The Examiner contends that it would have been obvious in view of Santini to place a metallic covering over the microneedles of Krulevitch in order to "prevent leakage of the reservoirs or contamination of the reservoirs contents" (Office Action, July 2, 2006, Page 3, ¶ 2) or so that "the device of Krulevitch would no longer be limited to molecules of a certain charge" (Office Action, July 2, 2006, Page 5, ¶ 5). This is hindsight-driven conjecture, unsupported by any objective evidence.

The Examiner's reading of Krulevitch is not how one or ordinary skill in the art would broadly and reasonably consider the reference, if read as a whole. Rather the Examiner's reading is unreasonably broad, based on improper hindsight reconstruction using Applicants' specification as a template, and is not properly based on reading Krulevitch as a whole.

In the instant case, a person of ordinary skill in the art trying to prevent contamination or carry molecules of a certain charge—the hypothetical problems or reasons imagined by the Examiner—has a nearly infinite variety of technical options to choose from in try to meet such objectives. For instance, the contamination means may be a seal located at the reservoir or at either or both ends of the microneedles, the means may utilize a mechanical or electromechanical valve, the means may focus on the formulation itself (e.g., making it less

fluid), or the means may involve rupturable or non-rupturable materials and operational designs, just to name of few of the myriad variables one skilled in the art might or might not utilize depending on a host of engineering and practical considerations. Accordingly, it would have required more than mere common sense for the artisan of ordinary skill to leap from the prior art teachings of Krulevitch, alone or in combination with Santini, to derive Applicants' particular claimed devices.

In fact, it is apparent that the combination posited by the Examiner is only obtained using ex post reasoning, because Krulevitch teaches completely different methods of both sealing, which would prevent contamination, and using molecules of a particular charge. Specifically, Krulevitch teaches that "channel sealing is dependent on selective poly (dimethylsiloxane) (PDMS) surface modifications," and that "[t]he polymer channel should be hydrophobic and pneumatic fluid should be hydrophilic when using hydrophilic reagents or vice versa... for [a] leak proof seal." (Col. 6, Lines 56-60) (emphasis added). Because Krulevitch teaches sealing molecules that are either hydrophilic or hydrophobic by the use of a specific type of polymer located in the substrate/channel structures, it teaches away from sealing with a metallic cover at the end of the microneedle.

A proper *prima facie* case of obviousness has not been established. Claims 19 and 42-47 are non-obvious over Krulevitch in view of Santini.

D. Ground No. 3

The rejection of claims 40 and 41 over Eppstein in view of Theeuwes is erroneous. A proper *prima facie* case of obviousness has not been established to support the rejection.

One of ordinary skill in the art would have had no reason to combine Theeuwes with Eppstein, and even if combined there is no reason apparent to one of ordinary skill in the art to

combine the known elements in the fashion claimed by Applicants. Eppstein does not teach the use of any expanding or shape changing material. Theeuwes discloses an osmotic system for delivering a beneficial agent over a prolonged period of time. Theeuwes does not remotely teach or suggest a device having either an array of discrete microtubes or a rupturable covering, and clearly does not suggest a *microtube* that has a *rupturable covering* that *encloses a first end of each reservoir*.

A person of ordinary skill in the art simply would not have combined Theeuwes with Eppstein for the reasons alleged by the Examiner. First, the Examiner has identified no evidence to suggest a specific market or design need to modify the teachings of Eppstein to omit electronics from the device. Second, there is no evidence that one of ordinary skill would be concerned with whether the Eppstein devices contains electronics, since the Eppstein devices are designed to operate in a patch placed outside the body (Example 6A, 6B, 6C, 7A, 7B, 7C, and 7D). Moreover, Applicants' claimed devices do not necessarily operate without electronics. Indeed, the Examiner has failed to articulate with any specificity why or how one of ordinary skill in the art would have been led to modify Eppstein's delivery device (which uses "pressure modulation activation links" to repeatedly modulate pressure in a plurality of microreservoirs) to somehow substitute an osmotic delivery system, which provides continuous pressure. Lastly, it is not predictable that one could achieve with the Theeuwes osmotic system the same control of release kinetics obtainable with the actuation means of Eppstein's device.

In sum, Theeuwes fails to supplement the deficiencies of Eppstein to meet all elements defining Applicants' claimed devices and methods. Accordingly, the combination of Theeuwes and Eppstein fails to establish a *prima facie* case of obviousness.

The cited prior art, as a whole, fails to teach the claimed combination of elements defining Applicants' claimed devices and methods. No *prima facie* case of novelty or obviousness has been established based on the references of record, alone or in combination. The rejections are therefore improper and must be withdrawn.

VIII. Claims Appendix

The appendix containing a copy of the claims involved in the appeal can be found on page 15.

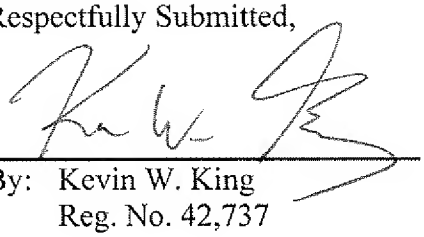
IX. Evidence Appendix

The appendix for evidence can be found on page 19. There is no evidence of record related to the appeal of the present application.

X. Related Proceedings Appendix

The appendix for related proceedings can be found at page 20. There are no appeals or interferences related to the appeal of the present application.

Respectfully Submitted,



By: Kevin W. King
Reg. No. 42,737

Date: December 28, 2007

SUTHERLAND ASBILL & BRENNAN LLP
999 Peachtree Street, NE
Atlanta, Georgia 30309-3996
Telephone: (404) 853-8068
Facsimile: (404) 853-8806

APPENDIX 1 – CLAIMS ON APPEAL

1-13. (Cancelled).

14. (Previously Presented) A device for the controlled release of chemical molecules comprising:

an array of discrete microtubes constructed of a metal or an alloy, each microtube comprising a reservoir defined therein;

a release formulation which comprises the chemical molecules, the release formulation being wholly contained in each reservoir;

a rupturable covering which closes an opening at a first end of each reservoir; and

a means for rupturing the rupturable covering and positively displacing the release formulation through the opening at the first end, to release the chemical molecules.

15. (Original) The device of claim 14, wherein the rupturable covering is provided with one or more defects to facilitate rupture.

16. (Original) The device of claim 14, wherein the means comprises a layer of an expanding material, and the release formulation is disposed between the layer of expanding material and the rupturable covering.

17. (Original) The device of claim 16, wherein a layer of a barrier material is disposed between the release formulation and the expanding material.

18. (Previously Presented) The device of claim 16, wherein the expanding material can be activated to expand upon application of heat.

19. (Previously Presented) A device for the controlled release of chemical molecules comprising:

an array of discrete microtubes, each microtube comprising a reservoir defined therein;

a release formulation which comprises the chemical molecules, the release formulation being disposed in each reservoir;

a rupturable covering enclosing a first end of each reservoir; and

a means for rupturing the rupturable covering and positively displacing the release formulation through an opening at the first end, to release the chemical molecules,

wherein the means for rupturing comprises a layer of an expanding material which can be activated to expand upon application of heat and a resistive heating element or resistive coating for heating the end of the microtube distal the rupturable covering upon application of an electric current through the resistive heating element or resistive coating, the release formulation being disposed between the layer of expanding material and the rupturable covering.

20. (Original) The device of claim 18, wherein the means for rupturing comprises a reactive coating over at least a portion of the end of the microtube distal the rupturable covering.

21. (Previously Presented) The device of claim 14, wherein at least a portion of the array of discrete microtubes is constructed of a shape memory alloy.

22. (Original) The device of claim 14, wherein the release formulation is contained in a rigid substructure within the reservoir.

23. (Original) The device of claim 14, wherein the release formulation is a drug formulation.

24. (Original) The device of claim 14, wherein the rupturable covering comprises a metal foil.

25. (Original) The device of claim 14, wherein the microtubes are connected by and extend from a planar base.

26. (Previously Presented) The device of claim 25, wherein the microtubes and the planar base are constructed of a biocompatible metal.

27. (Original) The device of claim 26, wherein the biocompatible metal is selected from the group consisting of titanium, gold, platinum, Nitinol, and stainless steel.

28. (Original) The device of claim 25, wherein the microtubes are fused to the planar base by an electroplating process, an electroless plating process, or by a brazing process.

29. (Previously Presented) The device of claim 25, wherein the planar base is joined to a metal package, which together enclose control electronics for controlling the means for rupturing.

30-34. (Cancelled).

35. (Original) A method for the controlled delivery of chemical molecules, comprising:

placing the device of claim 14 at a site for release of the chemical molecules; and

activating the rupturing means to rupture the rupturable covering and release the chemical molecules at the site.

36. (Original) The method of claim 35, wherein the chemical molecules comprise a drug and the site is *in vivo*.

37-38. (Cancelled).

39. (Previously Presented) The device of claim 14, wherein each microtube has an inner diameter of between about 0.5 mm and 1.0 mm.

40. (Previously Presented) The device of claim 16, further comprising a semipermeable membrane enclosing a second end of each reservoir distal the rupturable covering, the semipermeable membrane being operable to permit selected molecules from outside the reservoir to diffuse to the expanding material to cause the expanding material to expand and displace the release formulation in an amount effective to rupture the rupturable covering and discharge the release formulation from the reservoir.

41. (Previously Presented) The device of claim 40, further comprising a reservoir cap, which covers the semi-permeable membrane, and a means for selectively disintegrating the reservoir cap.

42. (Previously Presented) The device of claim 19, wherein the release formulation is a drug formulation.

43. (Previously Presented) The device of claim 19, wherein the rupturable covering comprises a metal foil.

44. (Previously Presented) The device of claim 19, wherein the rupturable covering is provided with one or more defects to facilitate rupture.

45. (Previously Presented) The device of claim 19, wherein the microtubes are constructed of titanium, gold, platinum, Nitinol, stainless steel, or another metal or alloy.

46. (Previously Presented) The device of claim 19, wherein the microtubes are connected by and extend from a planar base.

47. (Previously Presented) The device of claim 46, wherein the planar base is joined to a metal package, which together enclose control electronics for controlling the means for rupturing.

APPENDIX 2 – EVIDENCE

None.

APPENDIX 3 – RELATED PROCEEDINGS

None.